## REMARKS

Claims 1-3, 8, 10-13, 16-19, 36-39 and 48-58 were examined. In the instant Final Office Action, the Examiner has raised the following issues, which are set forth by number below in the order they are addressed herein:

1) Claim 1 is objected to as allegedly informal; and
2) Claims 1-3, 8, 10-12, 16-19, 36-39 and 53-57 stand rejected under 35 USC § 102(e), as allegedly anticipated by US Publication No. 2003/0185858 of Birkett (Birkett).

Applicants thank the Examiner for withdrawal of the rejections of the previous Office Action. Even so, Applicants hereby amend Claims 1, 8, 12 and 18, and cancel Claim 2, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments. Applicants reserve the right to prosecute the original, similar, or broader claims in one or more future application(s). These amendments do not introduce new matter.

### 1) The Claims Are Formal

The Examiner has objected to Claim 1 as allegedly informal for containing the phrases "linked to" and "inserted at." The Examiner states that this "language is internally inconsistent as linked to reads on conjugation, while inserted reads on fusions and chimers" (Final Office Action, page 4). Accordingly, Applicants hereby amend Claim 1, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). In particular, Applicants hereby amend Claim 1 to recite "comprising a heterologous antigen <u>inserted within</u> the amino acid sequence set forth in SEQ ID NO:38." As the amended claims are formal, Applicants respectfully request that this objection be withdrawn.

**2) The Claims Are Novel**

The Examiner has rejected Claims 1-3, 8, 10-12, 16-19, 36-39 and 53-57 under 35 USC § 102(e), as allegedly anticipated by US Publication No. 2003/0185858 of Birkett (Birkett). The Examiner states that:

> Birkett teaches immunogenic Hbc chimer particles stabilized with an N-terminal cysteine. Birkett also teaches HBc protein SEQ ID NO:38 (ADG63872; See SCORE Result 10, 38.rag) and immunogenic particles comprising the recombinant hepatitis core chimeric protein; further containing a heterologous epitope (up to 30 sequences [0035]); located N-terminally or C-terminally to the chimer particles [0030, 0031]; further comprising B cell epitope or T cell epitope [0074]; comprising residues at position 150 (end of residue 149) [0038]; in vaccines [0041]; further comprising woodchuck core antigen sequences [Fig. 1; 0073]0; as well as additional heterologous epitopes (such as two, to encode additional B cell epitopes or activating factors or enhancers) [0094] as well as the nucleic acids and vector encoding it [0201, 0202]; for humans [0044]; further including flanking glutamic acid and aspartic acid residues as linkers [0123].
>
> Birkett also teaches retention and inclusion of specific positions 75 and 85 in Domains I and II, respectively, for peptide bonding and linkage of heterologous epitopes [0110]; as well as zero to all residues of amino acids 76-85 ... linked to a heterologous epitope of one to 2456 amino acid residues (comprising heterologous epitopes 50 or fewer amino acids in length), thus teaching linkage to positions 76, 77, 78, 81, 82, 83 and 84 [0036] (Final Office Action, pages 5 and 6).

Although Applicants respectfully disagree that the claims are anticipated by Birkett, Applicants hereby amend Claims 1, 8, 12 and 18, and cancel Claim 2, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). In particular, Claims 1 and 18 are amended to recite insertion of a heterologous antigen at "a position chosen from amino acid residues 44, 71, 72, 73, 74, 75, 76, 77, 78, 81, 82, 83, 84, 85, ~~92, N-terminal or C-terminal~~ 92 of SEQ ID NO:38," to read upon woodchuck hepadna virus core antigen (WHcAg) fusions / chimeras comprising an internal peptide-bonded heterologous antigen. In addition, the original language of dependent Claim 12 has been restored.

Applicants strongly disagree that Birkett anticipates the claims. The Examiner is respectfully reminded that:

> [t]he disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation (MPEP 2121.01).[1]

Applicants contend that Birkett fails to provide any working examples describing how to make or use a hybrid WHcAg particle comprising a heterologous antigen and that absent Applicants' disclosure undue experimentation is required to produce the claimed invention. The actual and prophetic examples of Birkett are restricted to the disclosure of *human hepatitis B core antigens (HBcAg)* comprising heterologous amino acids peptide-bonded to a only a limited number of positions within HBcAg (e.g., *position E77, D78, N-terminal or C-terminal*). Birkett simply states "[l]ess preferred still are the sequences of woodchuck and ground squirrel at aligned positions 2 through 149" (Birkett, paragraph [0173]). Accordingly, Birkett was not in possession of non-human hepadnavirus core antigens and Birkett did not teach how to make or use a hybrid WHcAg particle comprising a heterologous antigen. Birkett's disclosure only amounts to an invitation to try. In contrast, Applicants believe they were the first to successfully prepare hybrid woodchuck hepatitis virus cores that assemble as hybrid particles.

The Examiner is also reminded that:

> [w]here a process for making the compound is not developed until after the date of invention, the mere naming of a compound in a reference, without more, cannot constitute a description of the compound (MPEP 2121.02).[2]

Applicants further contend that prior to development of the combinatorial technology provided in the present Application, a significant proportion of hybrid HBcAg (as well as WHcAg) cores could not be produced due to well-known problems in particle assembly (*See, e.g.,* Jegerlehner *et al., Vaccine*, 20:3104-3112, 2002 and Karpenko *et al., Amino Acids,* 18:329-337, 2000). Furthermore, not all hybrid HBcAg and WHcAg cores can be expressed, let alone assemble to properly present a heterologous antigen to an antibody. Birkett clearly illustrates this point in the parent application (US Patent Application

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[1] Referring to *Elan Pharm., Inc. v. Mayo Foundation for Medical and Education Research*, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003).

[2] Referring to *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968).

Publication No. 2003/0138769) when listing twenty "epitopes that have failed to express when inserted between D78 and P79 (V2) in a HBc chimer" (See, e.g., paragraph [0351] and Table 7). Similarly, Applicants have found that a truncated WHcAg having a $Cys^{150}$ carboxy-terminus did not assemble as hybrid particles when recombinantly expressed from multiple constructs: M epitope insert at position 74, CE epitope insert at position 74, HV-2 epitope insert at position 75, HV-3 epitope insert at position 74, HV-3 epitope insert at position 75, HV-4 epitope at position 74, CD40L immune enhancer insert at the carboxy-terminus, and IM2(-) insert at position 78 (Specification, Table 13 on page 102). However, these epitopes were successfully expressed and assembled as hybrid WHcAg particles when alternative C-termini were used. Altering the insert position and/or C-terminus to rescue hybrid particle assembly is one example of the utility of the combinatorial technology disclosed in the present application. US Publication No. 2003/0185858 of Birkett does not provide this teaching. In short, Applicants assert that Birkett does not enable the production and use of the woodchuck hepadna virus core antigen (WHcAg) fusions / chimeras comprising an internal peptide-bonded heterologous antigen (or the nucleic acids encoding the WHcAg fusions / chimeras) and as such does not anticipate the pending claims.

Moreover, Birkett does not anticipate Claims 38 and 39 since Birkett discloses the use of glutamic acid and aspartic acid residues as linkers for heterologous epitope conjugates, whereas these claims require acidic residues to flank the peptide-bonded heterologous antigen (Birkett, paragraph [0123]). As the prior art fails to provide the requisite enablement, and/or fails to describe all of the limitations, the pending claims are also not anticipated by Birkett. Accordingly, Applicants respectfully request that these rejections be withdrawn.

***PATENT***
Attorney Docket No. **VACCINE-07083**

## CONCLUSION

Applicants believe the amendments and arguments set forth above traverse the Examiner's rejections and, therefore request that a timely Notice of Allowance be issued in this case. However, should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect before the mailing of a further Office Action.

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